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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/783,268

02/20/2004

Andrea Savarino

97728.00147

7328

21832 7590 04/16/2008  
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EXAMINER

SAMALA, JAGADISHWAR RAO

ART UNIT

PAPER NUMBER

1618

MAIL DATE

DELIVERY MODE

04/16/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/783,268	<b>Applicant(s)</b> SAVARINO, ANDREA	
	<b>Examiner</b> JAGADISHWAR R. SAMALA	<b>Art Unit</b> 1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 22 January 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 12, 14, 28 and 31-37 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 12, 14, 28 and 31-37 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>08/05/2005; 03/15/2006; 12/06/2006 &amp; 01/31/2008</u> .     | 6) <input type="checkbox"/> Other: _____                          |



## **DETAILED ACTION**

### **Status of Application**

1. Acknowledgment is made of the amendment filed on 01/22/2008. Upon entering the amendment, claims 12, 14 and 28 are amended and claims 13, 29 and 30 are cancelled. Accordingly, pending claims are 12, 14, 28 and 31-37 and presented for examination.

### **Response to Arguments**

2. Applicant's arguments with respect to claims 12, 14, 28 and 31-37 have been considered but are moot in view of the new ground(s) of rejection. Previous rejections that are not reiterated herein are withdrawn.

### ***Claim Rejections - 35 USC § 103***

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claims 12 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cerami et al. (US 2002/0077271 A1) in view of Liversidge et al. (IS 6,221,400 B1) or Dong et al. (US 2002/0071863 A1).

Cerami et al discloses a method of administration of an effective amount of a pharmaceutical composition for treatment or prevention of infectious diseases, such as parasite and viral diseases, including, for e.g. malaria (caused by drug resistant plasmodium species) and acquired immunodeficiency syndrome in humans. (see abstract). And composition encompasses a class of alkyl aryl carbonyl compounds and an effective amount of an antimalarial drugs such as quinine, aminoquinolines (chloroquine and primaquine) pyrimethamine, mefloquine, halofantrine and artemisinins and the like (see para 0143).

Cerami et al meets the claims limitations but differs from the instant claims only in that Cerami does not include at least one inhibitors of the HIV protease for treating malaria.

[illegible]

Dong et al discloses a method of administering pharmaceutical composition comprising antiviral agents to a patient in need of antiviral therapy. And composition

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comprises antiviral drugs (protease inhibitors) such as saquinavir, adefovir, ritonavir, indinavir, nelfinavir, amprenavir, zidovudine and zalcitabin.

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate antiviral drugs (protease inhibitors) such as saquinavir, adefovir, ritonavir, indinavir, nelfinavir, amprenavir, zidovudine and zalcitabin in the pharmaceutical composition taught by Cerami. In view of Liversidge and Dong, motivation would come from the method treating viral infections either alone or in combination with other treatments.

When these references are taken together, one would have been motivated to extend Liversidge and Dong's teaching to add additional HIV protease inhibitors to maximize therapeutic efficacy. As suggested by cited references, one would have reasonably expected successful addition of active agents (HIV protease inhibitors) because the effectiveness, extra benefits (i.e. treatment of an infections disease with chemicals involves killing or inhibition of growth of the infectious agent, which may include free-living and parasitic organism that cause malaria) and safety are already well proven and are well suggested by latter references cited.

One would have been motivated to do so, with reasonable expectation of success because it is always desirable to have extended therapeutic modalities to improve patient's compliance by enhancing patient satisfaction and increasing the selection option. The techniques and skills required for making such substitution is conventional knowledge or well within the skills of ordinary artisan as evidenced by these references cited.

One would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same ingredients and share common utilities) and pertinent to the problem which applicant concerns about. MPEP 2141.01 (a).

4. Claims 12, 14, 28 and 31-37 rejected under 35 U.S.C. 103(a) as being unpatentable over Cerami et al. (US 2002/0077271 A1) in view of Liversidge et al. (IS 6,221,400 B1) or Dong et al. (US 2002/0071863 A1) as applied to claims 12 and 14 above, and further in view of Davis (US 5,278,173) and Johan et al (Biochemical Pharmacology, 61, 1531-1535, 2001).

Cerami in view of Liversidge or Dong meet the claim limitations as describe above but fails to include at least one quinoline antimalarial compound for treating HIV infection, malaria or both in humans.

Davis discloses a method of administering antimalarial drug to a human in an amount sufficient to prevent or at least inhibit infection of T lymphocytes by HIV in vivo or to prevent or at least inhibit replication of HIV in vivo (see col. 3, lines 4-8). And antimalarial drugs used for the treatment includes quinolinic compounds such as quinine, chloroquine, mefloquine, in the form of the free base or in the form of a pharmaceutically acceptable acid addition salt (see col. 4, lines 1-20). And further, the antimalarial drug is employed in an amount sufficient to provide an adequate concentration of the drug to prevent or at least inhibit infection of T lymphocytes by HIV in vivo (see co1.4, lines 65+).

Johan discloses that the addition of chloroquine to either hydroxyurea plus zidovudine AZT or to hydroxyurea plus didanosine further and equally inhibits HIV-1 replication as determined by RT activity. And this further reduction in HIV-1 replication due to chloroquin was observed both in recently and chronically HIV-1 infected T cells and monocytes, both in cell lines and in primary cells. The concentration of chloroquin that provides this additional activity is in the range of plasma concentrations that are reported in patients chronically treated with hydroxyl chloroquine for either rheumatic disease or the prevention of malaria ( see abstract and page 1534).

It would have been obvious to one of ordinary skill in the art at the time of the invention was made to modify the invention of Cerami in view of Liversidge or Dong to include at least one quinoline antimalarial compounds because Davis and Johan teaches that incorporation of antimalarial agents such as quinine, chloroquine, mefloquine or chloroquine in combination of zidovudine to provide an adequate concentration of drug to prevent or atleast inhibits HIV. In view of Davis and Johan, motivation would come from the method for treating HIV infections, malaria or both systematically.

Therefore, taken the teaching of the references together, one of ordinary skill in the art at the time the invention was made would have reasonable expectation of success that combination of antimalarial drugs (quinine, chloroquine, mefloquine) with the inhibitors of the HIV protease would provide the desired method of treating HIV infection, malaria or both in humans.



### **Conclusion**

1. No claims are allowed at this time.
2. Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAGADISHWAR R. SAMALA whose telephone number is (571)272-9927. The examiner can normally be reached on 8.30 A.M to 5.00 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571)272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/  
Supervisory Patent Examiner, Art Unit 1618

/Jagadishwar R Samala/  
Examiner, Art Unit 1618

sjr